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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/390,634	09/07/1999	PAUL J. PRICE	0942.4190002	7270

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/390,634	PRICE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-175* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-175* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of application 08/781,772, filed January 10, 1997, now abandoned.

Applicants' amendment filed February 10, 2004, has been received and entered. Claims 160 and 168 have been amended. Claims 174 and 175 have been added. Claims 89-175 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 160 and 168 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because it recited the trademark term 'Albumax^{R}' is withdrawn.

Amendments to the claims to delete the trademarked term and insert a more general description has obviated the basis of the rejection (also see Applicants' amendment, page 24, Section III).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 89-103, 105-111, 117-127, 129, 131, 133, 135, 137,139, 141, 143, 145, 147, 151, 153, 157-159, 161-164, 166, 167, 169-172 stand rejected and newly added claim 174 is rejected under 35 U.S.C. 102(b) as being anticipated by Ponting (US Patent 5,405,772).

Applicants summarize the requirements for anticipation under 35 USC 102 citing *In re Donohue* in support of their summary. Summarizing the instant invention as a serum-free eukaryotic cell culture medium supplement Applicants argue that Ponting does not anticipate the claimed invention because he teaches a "*complete media*", thus does not teach every element of the claim. See Applicants' amendment, bottom of page 24, Section IV. Applicants' arguments have been fully considered, but not found persuasive.

As noted in the previous office action the broad independent claims encompass a product comprising a basal cell culture medium and a serum-free eukaryotic culture medium supplement, use thereof in methods to culture embryonic stem cells, and compositions comprising the embryonic stem cell and the basal cell culture medium with a serum-free eukaryotic culture medium. To this end, Examiner agrees with Applicants general summary of the claimed invention. However, Examiner does not agree that this is in contrast to the teaching of Ponting. As in the present disclosure, Ponting defines the use of serum as a recognized problem in the art (see for example column 1, lines 25-32). Examiner would agree that the teaching of Ponting provides conditions for a "complete" media, however this is in the same context as presented in the present disclosure. Specifically, Ponting provides guidance for the specific elements to be added to standard or basal medium in lieu of serum. Even the instant specification defines the

present invention as providing "a substitute for the serum component of a **complete** medium" (page 15, lines 6-7, **emphasis added**). Applicants' arguments that the instant invention is different from that disclosed by Ponting is not found persuasive because both disclosures provide guidance for the addition of specific elements to substitute for absence of serum in a medium.

As noted in previous office action, Ponting teaches a medium for long term proliferation and development of cells. Beyond basal media commercially available, Ponting provides guidance for obtaining serum free media (starting at column 14, line 57) and teach the specific components and preferred ranges thereof to include in the media (see for example Table in columns 12 and 13). More specifically, Ponting teaches that the media can contain albumin (e.g. human or bovine), transferrin (e.g. human or bovine), growth factors, vitamins, antioxidants, insulin and various trace elements (see columns 9-10, tables and reduction to practice in working examples). Ponting teaches that the media disclosed can be used to culture a variety of cell types including embryonic stem cells (column 8, lines 13-15) including specific reference to known mouse embryonic stem cell lines. Further, Ponting teaches that general culturing methods known in the art can be used to culture a particular cell type, such as providing a feeder cell layer (column 8, lines 30-37). Finally, Ponting teaches that the cultured cells can be used in a variety of methods including in the production of proteins in culture (column 16, lines 21-31 and 45-64) and methods of differentiation (see column 8, lines 32-42, lines 61-69 and working examples). Applicants do not argue that any of these specific teachings or elements added to the basic medium by Ponting are different from that disclosed in the instant specification, only that the medium taught by Ponting is complete medium. This argument is not found persuasive because

both Ponting and the instant specification and claimed invention provide guidance to make a complete medium.

Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 89-173 and newly added claims 174 and 175 are rejected under 35 U.S.C. 103(a) as obvious over Ponting (US Patent 5,405,772) and Gibco BRL Products and Reference Guide ((1997) Chapters 5 and 8).

Applicants' summarize the requirements for establishing a *prima facie* case of obviousness citing *In re Royka, In re Glaug, In re Rijckaert, In re Rouffet* and *In re Dembiczak* in support of their summary (page 25) and argue that Ponting does not provide the elements recited

in the claims, nor if the elements exist as asserted by Examiner, any clear and particular motivation to combine them with the teachings of Ponting. See Applicants' amendment, bottom of pages 25-26, Section IV. Applicants' arguments have been fully considered as they apply to the new rejection.

The claims at issue are drawn to the addition of specific forms of albumin and transferrin, for example iron-saturated transferrin or lipid poor and recombinant albumin, as well as specific growth factors necessary for maintaining mouse embryonic stem cells in an undifferentiated state, such as the use of LIF. Additionally, the claims indicates that the media composition can be in a frozen state preparations. As argued above the invention disclosed by Ponting is to provide a completely defined media and teaches that the disclosed media can be used for variety of cell types and that the defined media 'makes possible the precise determination of the effect of a known molecule" Column 7, lines 44-50). Further, Ponting teaches that in determining the effective amount of any of the constituent components experimentation by methods known to a cell culturist would have to be done (bridging columns 8-9 and generally supported by the working examples). Finally, Ponting teaches that specific conditions for culturing a particular cell type would have to be adapted by substituting the serum-supplement to the methods and materials known in the art that would have been used for any particular cell type (starting in column 15, section E). As argued above, the teachings of Ponting anticipate claims 89-103, 105-111, 117-127, 129, 131, 133, 135, 137,139, 141, 143, 145, 147, 151, 153, 157-159, 161-164, 166, 167, 169-172 and 174.

Turning to the remaining claims, with respect to claims requiring that the composition be frozen (claim 104), Ponting specifically provides guidance on preserving the medium to reduce

damage from repeated freeze thaw (column 14, lines 60-62). Thus, while Ponting does not specifically teach to freeze the compositions, clearly this is a process commonly known in the art for preserving medium and makes obvious freezing the compositions for storage purposes and there is a reasonable expectation of success that such medium compositions can be frozen and successfully thawed for later use.

With respect to the specific compounds to be added to the media such as LIF, SF, lipid-poor albumin, iron-saturated transferring, it is noted that these elements were commercially available at the time of filing (for example page 15 of the instant specification). As a further demonstration that these elements exist and were used as cell culture agents, the Gibco BRL Products and Reference Guide is now cited as a secondary reference in the basis of the rejection. Examiner acknowledges that Ponting does not specifically teach to use such factors as LIF, iron-saturated transferrin or lipid poor and recombinant albumin, these factors were readily available at the time of filing and used in cell culturing.

In traverse of the prior rejection Applicants argue even if these elements were commonly known in the art, that there is no specific motivation to modify Ponting. This argument is not persuasive because beyond the design choice and optimization each of these components may offer in the culturing of cells there is specific motivation for particular elements as that would be known and would be required by one of skill in the art. For example, at the time of filing it was well known that mouse embryonic stem cells required LIF in the culture media to efficiently maintain their undifferentiated state during culturing, therefore, it would be obvious to include this factor in the propagation of embryonic stem cells. Further, if the mouse ES cells were to be used in methods of differentiation or if the culture was human embryonic stem cells which were

known not to be responsive to the presence or absence of LIF, this factor would be excluded from the media. Similarly, the source of albumin or transferring could be used based on the species of stem cell being cultured to provide maximum activity of the factor in the media. While the specification does not provide any specific teaching for use of any one of the components in any specific circumstance, the skilled artisan would be motivated to use each of these specific elements in the media in order to optimize the growth and culturing conditions for any given method.

As noted above, the teaching of Ponting anticipates the specific embodiments encompassed by claims 89-103, 105-111, 117-127, 129, 131, 133, 135, 137,139, 141, 143, 145, 147, 151, 153, 157-159, 161-164, 166, 167, 169-172, and though Ponting does not specifically disclose the specific components listed in the remaining claims, the use of these components would be obvious because they are factors commonly used in cell culture. Further, Ponting teaches that the media should be as defined as possible and optimized for a given cell type, therefore one would be motivated to use and test the various forms of these components for their specific affects on the cells in culture. For example lipid-poor albumin provides a more defined source of albumin, lacking lipids that could affect the cells. Moreover, Ponting teaches that the components can be natural or synthetic (column 11, lines 65-68), wherein a synthetic component would represent a more defined molecule free from potential contaminants that may be present in naturally isolated sources. The level of knowledge and skill in the art for culturing cells is high, and there would be a reasonable motivation and expectation of success to use specific components from various sources as generally taught by Ponting to provide for a more defined and optimized media. Upon review of the present specification, there is no specific teaching

that any one of the components recited or encompassed by the instant claims provides any unexpected affect on the cultured cells that would not have been readily known in the art, such as the use of LIF or feeder cells to maintain embryonic stem cells in culture.

Thus, for the reasons above, the claimed invention as a whole was clearly *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Atsumi *et al.* Develop. Growth & Differ. 35(1):81-87 (1993) provides further evidence that at the time of filing and issuance of Ponting serum-free conditions for culturing embryonic stem cells were known and used. Atsumi *et al.* teach to use as a serum supplement serum-free media that are obtained as a conditioned media. Using such media Atsumi *et al.* were able to define specific factors supplied by the feeder cells in order to make a complete serum-free media.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach